WHAT IS CLAIMED IS:

1. A method of producing a lysosomal hydrolase having an oligosaccharide modified with N-acteylglucosamine-1-phosphate comprising
    a. contacting a mammalian cell culture expressing a lysosomal hydrolase with a mutagenic agent;
    b. culturing said mammalian cell culture in the presence of *Pseudomonas* exotoxin A in an amount sufficient to select for cells resistant to the *Pseudomonas* exotoxin A;
    c. selecting said cells resistant to *Pseudomonas* exotoxin A; and
    d. isolating said lysosomal hydrolase having an N-acteylglucosamine-1-phosphate from said resistant cells.
2. The method of Claim 1, wherein said lysosomal hydrolase is selected from the group consisting of α-glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase , N-acetylgalactosamine-6-sulfatase or β -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β-glucuronidase, Heparan N-sulfatase, N-Acetyl-α-glucosaminidase, Acetyl CoA-α-glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase, Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, Arylsulfatase A Cerebroside, Ganglioside, Acid β-galactosidase G_{M1} Galglioside, Acid β-galactosidase, Hexosaminidase A, Hexosaminidase B, α-fucosidase, α-N-Acetyl galactosaminidase, Glycoprotein Neuraminidase,

Aspartylglucosamine amidase, Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and Sphingomyelinase.

3. The method of Claim 1, further comprising contacting said lysosomal hydrolase having an N-acteylglucosamine-1-phosphate with an active GlcNAc-phosphotransferase.

4. The method of Claim 3,wherein said phosphodiester α-GlcNAcase comprises an amino acid 56 to 515 of SEQ ID NO:18.

5. The method of Claim 3, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

6. The method of Claim 3, further comprising purifying said glycoprotein after said contacting.

7. The method of Claim 1, wherein said mutagenic agent is a chemical mutagenic agent.

8. The method of Claim 7, wherein said mutagenic agent is ethyl methane sulfonate.

9. The method of Claim 1, further comprises culturing said mammalian cell culture in the presence of a α 1,2-mannosidase inhibitor.

10. The method of Claim 9, wherein said a α 1,2-mannosidase inhibitor comprises both deoxymannojirimycin and kifunensine.

11. A method of producing a lysosomal hydrolase having an oligosaccharide modified with N-acteylglucosamine-1-phosphate comprising

a. introducing a polynucleotide sequence encoding the lysosomal hydrolase in a furin deficient mammalian cell;

b. culturing said furin deficient mammalian cell containing the polynucleotide sequence encoding the lysosomal hydrolase for a time and under conditions suitable for expression of the lysosomal hydrolase; and

c. collecting the lysosomal hydrolase expressed.

12. The method of Claim 11, wherein said lysosomal hydrolase is selected from the group consisting of α-glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase , N-acetylgalactosamine-6-sulfatase or β -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β-glucuronidase, Heparan N-sulfatase, N-Acetyl-α-glucosaminidase, Acetyl CoA-α-glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase, Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, Arylsulfatase A Cerebroside, Ganglioside, Acid β-galactosidase G_{M1} Galglioside, Acid β-galactosidase, Hexosaminidase A, Hexosaminidase B, α-fucosidase, α-N-Acetyl galactosaminidase, Glycoprotein Neuraminidase, Aspartylglucosamine amidase, Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and Sphingomyelinase.

13. The method of Claim 11, further comprising contacting said lysosomal hydrolase having an N-acteylglucosamine-1-phosphate with an active GlcNAc-phosphotransferase.

14. The method of Claim 13,wherein said phosphodiester α-GlcNAcase comprises an amino acids 56 to 515 of SEQ ID NO:18.

15. The method of Claim 13, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

16. The method of Claim 13, further comprising purifying said glycoprotein after said contacting.

17. The method of Claim 11, further comprises culturing said mammalian cell culture in the presence of a α 1,2-mannosidase inhibitor.

18. The method of Claim 17, wherein said a α 1,2-mannosidase inhibitor comprises both deoxymannojirimycin and kifunensine.

19. A method of producing a lysosomal hydrolase having an oligosaccharide N-acteylglucosamine-1-phosphate comprising

a. a step for expressing a lysosomal hydrolase in a furin deficient mammalian cell; and

b. a step for collecting the lysosomal hydrolase expressed.

20. The method of Claim 19, wherein said lysosomal hydrolase is selected from the group consisting of α-glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase , N-acetylgalactosamine-6-sulfatase or β -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β-glucuronidase, Heparan N-sulfatase, N-Acetyl-α-glucosaminidase, Acetyl CoA-α-glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase,

Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, Arylsulfatase A Cerebroside, Ganglioside, Acid β-galactosidase G_{M1} Galglioside, Acid β-galactosidase, Hexosaminidase A, Hexosaminidase B, α-fucosidase, α-N-Acetyl galactosaminidase, Glycoprotein Neuraminidase, Aspartylglucosamine amidase, Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and Sphingomyelinase.

21. The method of Claim 18, further comprising a step for removing the N-acetylglucosamine from said lysosomal hydrolase.

22. The method of Claim 21, further comprising a step for purifying said lysosomal hydrolase.

23. A method of producing a phosphodiester α-GlcNAcase comprising

a. contacting a mammalian cell culture expressing said phosphodiester α-GlcNAcase with a mutagenic agent;

b. culturing said mammalian cell culture in the presence of *Pseudomonas* exotoxin A in an amount sufficient to select for cells resistant to the *Pseudomonas* exotoxin A;

c. selecting said cells resistant to *Pseudomonas* exotoxin A; and

d. isolating said phosphodiester α-GlcNAcase having a pro-peptide from said resistant cells.

24. The method of Claim 23, wherein said mutagenic agent is a chemical mutagenic agent.

25. The method of Claim 24, wherein said mutagenic agent is ethyl methane sulfonate.

26. The method of Claim 23, wherein said phosphodiester α-GlcNAcase comprises SEQ ID NO:18.

27. The method of Claim 23, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

28. A method of producing a phosphodiester α-GlcNAcase comprising

a. culturing a furin deficient mammalian cell expressing said phosphodiester α-GlcNAcase for a time and under conditions suitable for expression of the phosphodiester α-GlcNAcase ; and

b. collecting the lysosomal hydrolase expressed.

29. The method of Claim 28, wherein said phosphodiester α-GlcNAcase comprises SEQ ID NO:18.

30. The method of Claim 28, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

31. A method of producing a phosphodiester α-GlcNAcase comprising

a. a step for expressing said phosphodiester α-GlcNAcase in a furin deficient mammalian cell; and

b. a step for collecting the phosphodiester α-GlcNAcase expressed.

32. The method of Claim 31, wherein said phosphodiester α-GlcNAcase comprises SEQ ID NO:18.

33. The method of Claim 32, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

34. A method of producing a lysosomal hydrolase having an oligosaccharide modified N-acteylglucosamine-1-phosphate comprising

a. culturing a mammalian cell in the presence of *Pseudomonas* exotoxin A in an amount sufficient to select for cells resistant to the *Pseudomonas* exotoxin A;

b. selecting said cells resistant to *Pseudomonas* exotoxin A; and

c. isolating said lysosomal hydrolase having an N-acteylglucosamine-1-phosphate from said resistant cells.

35. The method of Claim 34, wherein said lysosomal hydrolase is selected from the group consisting of α-glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase , N-acetylgalactosamine-6-sulfatase or β -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β-glucuronidase, Heparan N-sulfatase, N-Acetyl-α-glucosaminidase, Acetyl CoA-α-glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase, Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, Arylsulfatase A Cerebroside, Ganglioside, Acid β-galactosidase G_{M1} Galglioside, Acid β-galactosidase, Hexosaminidase A, Hexosaminidase B, α-fucosidase, α-N-Acetyl galactosaminidase, Glycoprotein Neuraminidase,

Aspartylglucosamine amidase, Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and Sphingomyelinase.

36. The method of Claim 34, further comprising contacting said lysosomal hydrolase having an N-acteylglucosamine-1-phosphate with an active GlcNAc-phosphotransferase.

37. The method of Claim 36,wherein said phosphodiester α-GlcNAcase comprises an amino acid 56 to 515 of SEQ ID NO:18.

38. The method of Claim 36, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.

39. The method of Claim 36, further comprising purifying said glycoprotein after said contacting.

40. The method of Claim 34, further comprises culturing said mammalian cell culture in the presence of a α 1,2-mannosidase inhibitor.

41. The method of Claim 40, wherein said a α 1,2-mannosidase inhibitor comprises both deoxymannojirimycin and kifunensine.

42. A method of producing a phosphodiester α-GlcNAcase comprising

a. culturing said mammalian cell culture in the presence of *Pseudomonas* exotoxin A in an amount sufficient to select for cells resistant to the *Pseudomonas* exotoxin A;

b. selecting said cells resistant to *Pseudomonas* exotoxin A; and

c. isolating said phosphodiester α-GlcNAcase having a pro-peptide from said resistant cells.

43. The method of Claim 42, wherein said phosphodiester α-GlcNAcase comprises SEQ ID NO:18.

44. The method of Claim 42, wherein said phosphodiester α-GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.